REMARKS

Applicants have amended Claim 18 to limit R^1 of the starting material to chlorine and of the product to chlorine and fluorine and to limit R^2 to hydrogen. The amendment in this respect is fully supported in the specification, including the examples. [In particular, Examples 1 and 3 teach the preparation of products in which a $-CHCl_2$ group is converted to a $-CHF_2$), whereas Example 2 teaches the preparation of a product in which a $-CHCl_2$ group is converted to a –CHClF group.] Applicants have also amended Claim 18 to remove the now redundant reference in the definition of group A to a "5-membered heterocycle" (in view of the previous narrowing to pyrazoles) and to limit the fluorinating agent to three reagent types.

Applicants have similarly amended Claim 19 to limit the definitions of R^1 and R^2 as they apply to formula (II) and to modify the definition of group A to refer to a pyrazole for consistency with amended Claim 18.

Applicants accordingly have amended Claim 20 to emphasize that the definition of R^1 relates to the starting material of formula (II) (as opposed to the product of formula (I)) and have amended Claim 21 to remove the now redundant definitions of R^1 and R^2. All claims remain fully supported in the specification.

Information Disclosure Statement

Applicants gratefully acknowledge the statement in the Office Action that the Examiner has considered their previously submitted Information Disclosure Statement. However, since the documents listed in Form PTO 1449 were not initialed, Applicants respectfully request that the Examiner provide an initialed copy with her next correspondence.

Rejection under 35 U.S.C. 112

Claims 25 and 26 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite with respect to the phrase "that it is carried." As kindly suggested by the Examiner, Applicants have amended each claim to read "that is carried" and respectfully submit that they have traversed this rejection.

Rejection under 35 U.S.C. 102

Claims 18-20, 22, 25, and 26 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,417,361 ("Hayashi et al"). Applicants respectfully traverse.

Hayashi et al discloses fluorinating compositions containing **(a)** hydrogen fluoride and **(b)** compounds that are liquid at 25°C and 1 atmosphere pressure and

have a boiling point of at least 120°C (and preferably having a pK_a of at least 12). E.g., column 1, line 66, through column 2, line 24. Suitable liquid compounds for use as the second component are identified in the reference at column 2, line 50, through column 4, line 55, as including an array of ureas (e.g., formulas (1), (2), (3), (4), and (5)), amides (e.g., formulas (6), (7), (8), and (9)), ethers (e.g., formulas (10) and (11)), esters (e.g., formulas (12) and (13)), and phosphoramides (e.g., formula (14)). Hayashi et al also teaches that the disclosed fluorinating compositions can be used **(i)** to fluorinate compounds of the formula $R_{14}[C(X_1)_3]_m$ (i.e., formula (15)) in which R_{14} can be alkyl, alkoxy, aryl, or aryloxy (but not heterocyclyl), each of the three X_1 groups is hydrogen or any halogen as long as the X_1 groups are not limited to being only hydrogen and/or fluorine (such as CH_3 or CF_3), and m is 1 to 6, to form compounds of formula $R_{14}[CF_n(X_2)_{3-n}]_m$ (i.e., formula (16)) in which X_2 is hydrogen or any halogen other than fluorine and n is 1 to 3 (see column 4, line 63, through column 5, line 15) or **(ii)** to fluorinate compounds of the formula $R_{15}[C(X_1)_3]_m$ (i.e., formula (17)) in which R_{15} is a heterocyclic aromatic group (including pyrazoles), each of the three X_1 groups is hydrogen or any halogen as long as the X_1 groups are not limited to being only hydrogen and/or fluorine (such as CH_3 or CF_3), and m is 1 to 9 to form compounds of formula $R_{15}[CF_n(X_2)_{3-n}]_m$ (i.e., formula (18)) in which X_2 is hydrogen or any halogen other than fluorine and n is 1 to 3 (see column 5, line 16, through column 6, line 55).

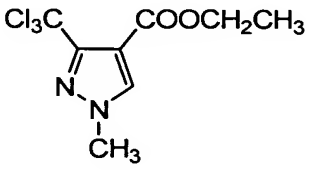
With respect to the non-aromatic compounds of alternative (i) of Hayashi et al, Applicants submit that the reference is clearly not anticipatory or suggestive of their claimed invention. With respect to the heteroaromatic compounds of alternative (ii), Hayashi et al at first glance might appear to be relevant because the formula $R_{15}[C(X_1)_3]_m$ can be read broadly as encompassing "pyrazole-$CHCl_2$" and the formula $R_{15}[CF_n(X_2)_{3-n}]_m$ can be read broadly as encompassing "pyrazole-CHClF" or "pyrazole-CHF_2 ." However, Applicants submit that these broad readings are not sufficient to anticipate their claimed invention.

First, Hayashi et al does not teach that amines or pyridine would be suitable for use as the second component of the disclosed fluorinating compositions. Although the physical state criteria set forth in the reference do not expressly exclude such compounds, Hayashi et al at column 1, lines 42-52, specifically teaches that complexes of HF and Lewis bases – with specific reference to complexes of HF with pyridine (i.e., Olah's reagent) or with triethylamine – are

"difficult to control in the preparation step due to a considerable exothermic reaction" and "are difficult to use in industry in view of recovery and reuse." Hayashi et al clearly teaches that the compositions it discloses and claims serve a stated purpose of overcoming the deficiencies of amine-containing fluorinating agents by being fluorinating agents that are "easy to handle and can be conveniently used." E.g., column 1, lines 53-62. In fact, as mentioned above, Hayashi et al describes in great detail the advantageous use of fluorinating agents containing certain ureas, amides, ethers, esters, and phosphoramides but not one amine. In view of the stated advantages of the fluorinating agents of the reference over amine-containing fluorinating agents (at least with respect to fluorination of compounds of formulas (16) and (18)), Applicants submit that Hayashi et al cannot reasonably be read to teach or even suggest that amine-containing fluorinating agents would be suitable for fluorinating pyrazole-containing compounds of formula (18) or, for that matter, the more narrowly defined pyrazole compounds of Applicants' formula (I). In the face of such contrary teachings, Applicants were able to obtain excellent results using fluorinating compositions based on aliphatic amines and pyridine to fluorinate the compounds of their formula (I).

Even if (solely for the sake of discussion) one were to ignore the deficiencies of amine-containing fluorinating agents as taught by Hayashi et al, it should be noted that two of the amines present in Applicants' specified fluorinating agents do not satisfy the 120°C minimum boiling point criterion specified by Hayashi et al. More specifically, $N(Et)_3$ (i.e., triethylamine) has a boiling point of 89-90°C and pyridine has a boiling point of 115-116°C. Furthermore, the amines specified by Applicant do not satisfy the stated preference in the reference for a pK_a of at least 12. See column 7, lines 15-16. Clearly, those skilled in the art would not be led by Hayashi et al to Applicants' claimed invention.

Second, even though Hayashi et al discloses an ester-containing pyrazole represented by the following formula



(e.g., column 15, lines 37-45, as well as by name in Example 23 at column 22), the disclosed compound bears a CCl_3 substituent that is converted to a CF_3 substituent,

not a $CHCl_2$ substituent that is converted to a CHClF or CHF_2 substituent as claimed by Applicants. It is well known that conversion of CCl_3 groups to CF_3 groups is accomplished much more easily than conversion of $CHCl_2$ groups to CHF_2 groups. In fact, it is known that CCl_3 groups can be preferentially converted to CF_3 groups in the presence of unaltered $CHCl_2$ groups. See M. Hudlicky, "Methods for Introducing Fluorine" in *Chemistry of Organic Fluorine Compounds*, Second Revised Edition (1976), page 96 (reaction 170 and preceding sentence) (copy enclosed). Furthermore, Hayashi et al does not provide any examples to show that the disclosed methods would accomplish the conversion of $CHCl_2$ groups to CHClF or CHF_2 groups under the conditions taught. Nevertheless, the Office Action at page 5 (as well as page 7 within the obviousness rejection) refers to Example 23 of the reference to support this rejection. Even if one ignores the known differences in reactivities of CCl_3 and $CHCl_2$ groups and the absence of any examples in Hayashi et al showing conversion of $CHCl_2$ groups to CHF_2 groups, Applicants submit that Example 23 is sufficiently flawed that it cannot be relied upon for any useful teaching. Example 23 teaches that the subject pyrazole compound was mixed with "0.4 g (235 m mol as HF)" without indicating what fluorinating agent was used to provide the HF. Moreover, none of the fluorinating agents used in the other examples could provide 235 mmol of HF equivalent if 0.4 g were used. (Even HF itself, with a molecular weight of 20, would provide only 20 mmol.) The failure of the example to disclose a fluorinating agent or a technically reasonable amount of any known fluorinating agent renders this example fatally flawed. And even if all of the above arguments were to be ignored and one were to accept (again, despite teachings of the literature to the contrary) that the fluorinating agents taught by Hayashi et al could convert $CHCl_2$ groups to CHClF or CHF_2 groups, Applicants maintain that the reference would not provide relevant insight into the use of amine- or pyridine-based fluorinating agents in the manner they now claim.

In view of the failure of the reference to teach the use of fluorinating agents containing an amine or pyridine as required by Applicants or to carry out the specific conversion specified by Applicants, Applicants respectfully submit that Hayashi et al does not anticipate their invention as claimed.

Rejection under 35 U.S.C. 103

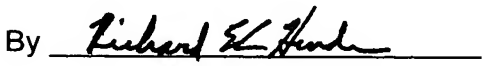
Claims 18-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hayashi et al. Applicants respectfully traverse.

As discussed above, Hayashi et al discloses fluorinating agents containing hydrogen fluoride in combination with a liquid compound having boiling points above 120°C. The Office Action at pages 6-7 relies at least in part on a supposed analogy between the fluorinating agents disclosed in the reference and those specified by Applicants. However, as discussed above, Hayashi et al does not teach or suggest that an amine or pyridine could be used as the second component of the disclosed fluorinating agents (and in fact specifically teaches the general deficiencies of fluorinating agents containing Lewis bases such as amines or pyridine) and does not teach that the compositions it does disclose would effectively convert $CHCl_2$ groups of ester-containing pyrazoles to CHClF or CHF_2 groups.

Applicants therefore respectfully submit that their invention as claimed is not rendered obvious by Hayashi et al.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

By 

Richard E. L. Henderson
Attorney for Applicants
Reg. No. 31,619

Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709
Phone No.: (919) 549-2183
Facsimile No.: (919) 549-3994
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Chemistry of Organic Fluorine Compounds

A LABORATORY MANUAL
WITH COMPREHENSIVE LITERATURE COVERAGE

Second Revised Edition

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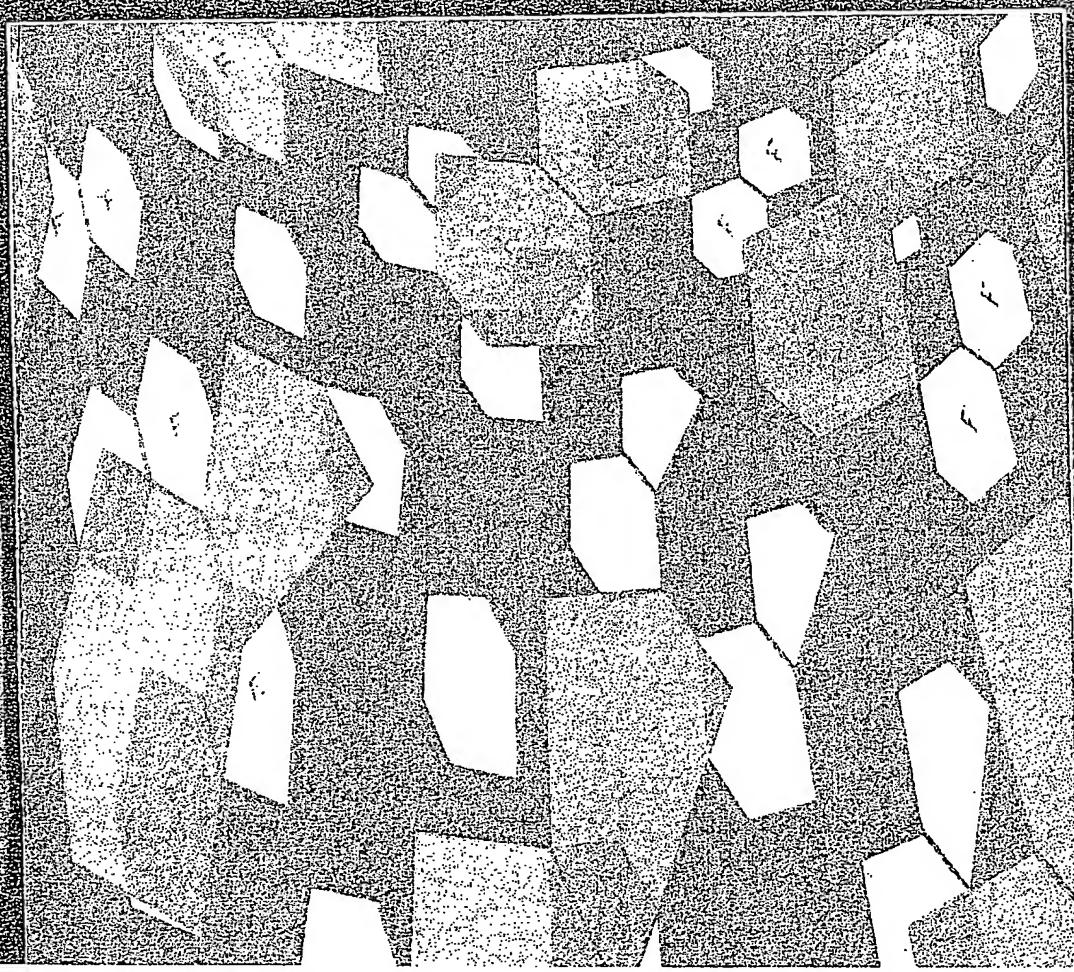


(1976)

von S. Pazenok JCS 03-3090

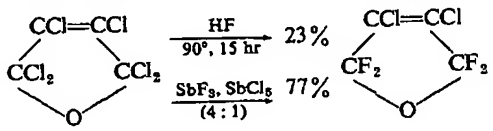
dine series, hydrogen fluoride replaces chlorine atoms in α- and γ-positions which are activated for nucleophilic displacement [*297a*, *348a*].

165 [*1373*]

$$CH_3CCl{=}CHCH_2CH(CO_2C_2H_5)_2 \xrightarrow[20°]{HF} CH_3CF_2CH_2CH_2CH(CO_2C_2H_5)_2\ 58\%$$

A very smooth replacement is that of halogens attached to a carbon alpha to a double bond [*354a*, *740a*] or to an aromatic ring. The conversion of benzotrichloride to benzotrifluoride has been achieved by means of anhydrous hydrogen fluoride over a very broad range of temperatures and with very good yields [*399*, *2439*, *2446*]. Similar results have been obtained with chlorinated homologs of benzene [*1918*] and pyridine [*1687*].

166 [*740a*]



167 [*2446*]

$$\xrightarrow{HF,\ 0°} 75\text{–}95\%$$

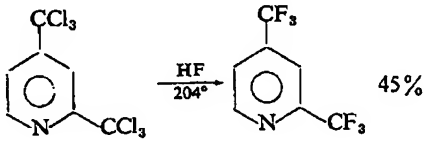
[*2439*]

$$C_6H_5CCl_3 \xrightarrow{HF,\ 40°,\ 1\cdot5\ atm.} 70\text{–}75\%\ C_6H_5CF_3$$

[*399*]

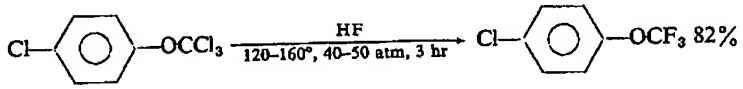
$$\xrightarrow{HF,\ 0° \rightarrow 135\text{–}140°,\ 15\ atm} 89\%$$

168 [*1687*]



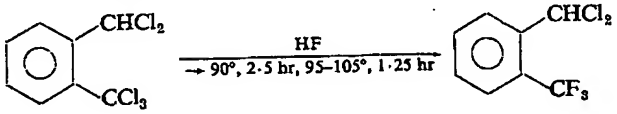
Trichloromethyl groups linked to an ether oxygen are also very reactive toward hydrogen fluoride and can easily be converted to trifluoromethyl derivatives [*815*].

169 [*815*]



Trichloromethyl groups are attacked by hydrogen fluoride preferentially over dichloromethyl groups [*840*] and over an acyl chloride grouping [*1648*].

170 [*840*]



[*1648*]

171